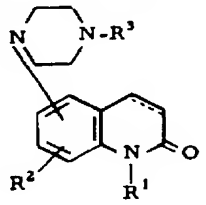
62119 K/26 B02 SAKA 11.11.81 *J5 8083-677
OTSUKA PHARM KK
11.11.81-JP-181360 (19.05.83) A61k-31/49 C07d-215/38

Carbostyril derivatives - having positive inotropic action, useful as cardiotonics

C83-060275

Carbostyril derivs. of formula (I) and their salts are new:



(I)

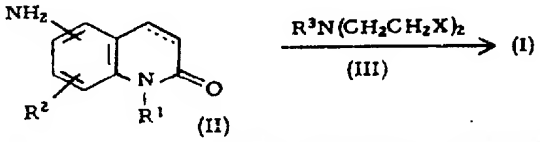
(R^1 is H, lower alkyl, lower alkenyl, lower alkynyl or phenyl-lower alkyl;
R^2 is H or lower alkoxy;
R^3 is H, lower alkanoyl, furoyl, pyridylcarbonyl, lower alkanesulphonyl, lower alkoxycarbonyl, lower alkoxycarbonyl-lower alkyl, phenylsulphonyl (opt. having lower alkyl as substitution gp. on phenyl ring), lower alkyl, lower alkenyl, lower alkynyl, phenylcarbonyl, phenyl-lower alkyl or phenyl-lower alkanoyl;
the phenyl ring of the above phenylcarbonyl, phenyl-lower alkanoyl and phenyl-lower alkanoyl may be substd. by lower alkylenedioxy or 1-3 gps. selected from lower alkoxy, halogen, lower alkyl, cyano, nitro, amino, OH, lower alkanoylamino, lower alkylthio and lower alkanoyloxy).

USES

(I) have myocardial hypersystole action (positive inotropic action) and coronary hyperkinemic action. They are useful as cardiotonics for therapy of cardiopathy such as congestive heart failure.

PREPARATION

(a)



(II) (III) (I)

(X is halogen, lower alkanesulphonyloxy, arylsulphonyloxy, aralkylsulphonyloxy or OH).

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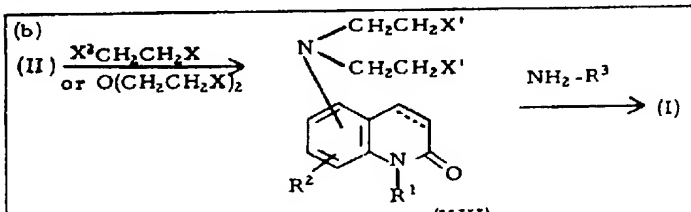
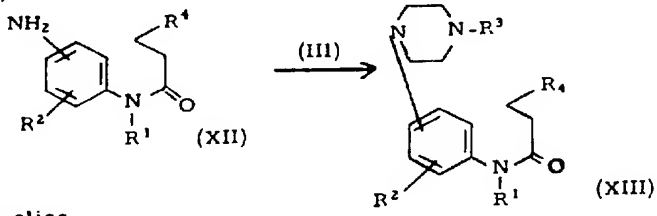
(b)



(VIII)

(X^2 is halogen; X' is as X, or the two X' gps. together form O).

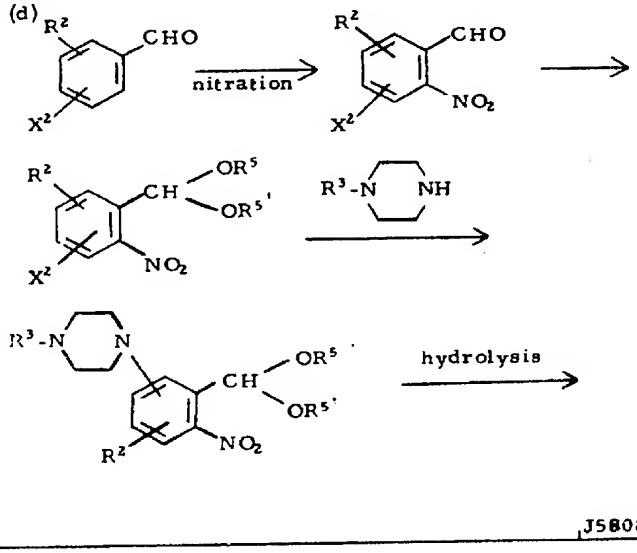
(c)



(XII) (XIII)

cyclise → (I; 3(4) satd.)

(d)



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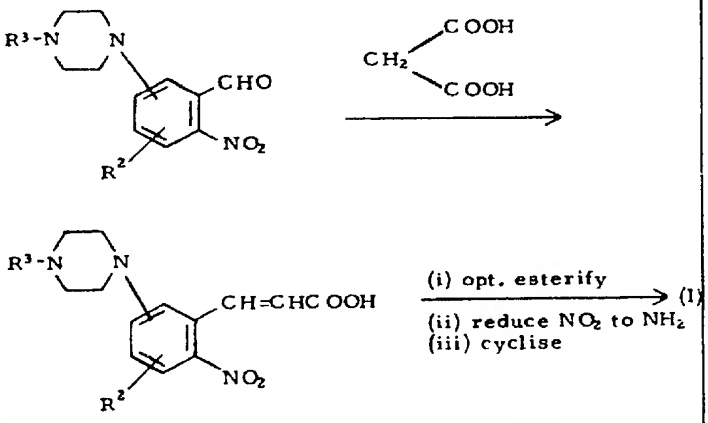
(e) Various interconversions are possible. E.g. (I; R^3 = H) may be acylated or alkylated etc., (I; R^1 = H) may be alkylated or the 3(4) bond may be converted by (de)hydrogenation



(R^5 and $R^{5'}$ are alkyl or together form alkylene).

(50ppW69DwgNo0/0).